



**EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastrointestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006**

**EFSA Publication**

*Link to article, DOI:*  
[10.2903/j.efsa.2012.2801](https://doi.org/10.2903/j.efsa.2012.2801)

*Publication date:*  
2012

*Document Version*  
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

*Citation (APA):*  
EFSA Publication (2012). *EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastrointestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006*. European Food Safety Authority. the EFSA Journal Vol. 10(7) No. 2801 <https://doi.org/10.2903/j.efsa.2012.2801>

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## SCIENTIFIC OPINION

### Scientific Opinion on the substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006<sup>1</sup>

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)<sup>2,3</sup>

European Food Safety Authority (EFSA), Parma, Italy

#### ABSTRACT

Following an application from Lesaffre International/Lesaffre Human Care, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of France, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort. The food constituent that is the subject of the health claim, *S. cerevisiae* var. *boulardii* CNCM I-3799, is sufficiently characterised. The claimed effect, reduction of gastro-intestinal discomfort, is a beneficial physiological effect. The target population proposed by the applicant is subjects from 18 to 74 years old with bowel discomfort. The Panel notes that none of the studies provided for the substantiation of the claim was conducted with the strain which is the subject of the claim (*S. cerevisiae* var. *boulardii* CNCM I-3799), except for two animal studies and one *in vitro* study. Upon an EFSA request, the applicant indicated that the rest of the studies provided were conducted with the strain produced by Biocodex Laboratories (*S. cerevisiae* var. *boulardii* HANSEN CBS 5926). The applicant also stated that the strain, which is the subject of the claim, *S. cerevisiae* var. *boulardii* CNCM I-3799, is equivalent to *S. cerevisiae* var. *boulardii* HANSEN CBS 5926, based on a comparative PCR inter-delta element analysis of both strains provided in the application. The Panel considered that the evidence provided was insufficient to establish that the strains *S. cerevisiae* var. *boulardii* CNCM I-3799 and HANSEN CBS 5926 are identical and, upon EFSA request for further information, additional evidence was not provided by the applicant. A cause and effect relationship cannot be established between the consumption of *S. cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort. © European Food Safety Authority, 2012

#### KEY WORDS

*Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799, gastro-intestinal discomfort, health claims.

<sup>1</sup> On request from the Competent Authority of France following an application by Lesaffre International/Lesaffre Human Care, Question No EFSA-Q-2012-00271, adopted on 27 June 2012.

<sup>2</sup> Panel members: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Monika Neuhäuser-Berthold, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Daniel Tomé, Hendrik van Loveren and Hans Verhagen. One member of the Panel did not participate in the discussion on the subject referred to above because of potential conflicts of interest identified in accordance with the EFSA policy on declarations of interests. Correspondence: [nda@efsa.europa.eu](mailto:nda@efsa.europa.eu)

<sup>3</sup> Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen for the preparatory work on this scientific opinion.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006. EFSA Journal 2012;10(7):2801. [9 pp.]. doi:10.2903/j.efsa.2012.2801. Available online: [www.efsa.europa.eu/efsajournal](http://www.efsa.europa.eu/efsajournal)

## SUMMARY

Following an application from Lesaffre International/Lesaffre Human Care, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of France, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence, including a request for the protection of proprietary data.

The food constituent that is the subject of the health claim is *S. cerevisiae* var. *boulardii* CNCM I-3799. The Panel considers that *S. cerevisiae* var. *boulardii* CNCM I-3799 is sufficiently characterised.

The claimed effect is reducing gastro-intestinal discomfort. The target population proposed by the applicant is subjects from 18 to 74 years old with bowel discomfort. The Panel considers that reducing gastro-intestinal discomfort is a beneficial physiological effect.

None of the studies provided for the substantiation of the claim were conducted with the strain that is the subject of the claim (*S. cerevisiae* var. *boulardii* CNCM I-3799), except for two animal studies and one *in vitro* study. Upon EFSA's request for further information, the applicant indicated that the rest of the studies provided were conducted with the strain produced by Biocodex Laboratories (*S. cerevisiae* var. *boulardii* HANSEN CBS 5926), sold under different brands. The applicant also stated that the strain, which is the subject of the claim, *S. cerevisiae* var. *boulardii* CNCM I-3799, is equivalent to *S. cerevisiae* var. *boulardii* HANSEN CBS 5926, based on a comparative PCR inter-delta element analysis of both strains, provided in the application. The Panel considered that the evidence provided was insufficient to establish that the strains *S. cerevisiae* var. *boulardii* CNCM I-3799 and HANSEN CBS 5926 are identical and, upon EFSA's request for further information, additional evidence was not provided by the applicant. The Panel also considered that in the absence of human data the two animal studies and one *in vitro* study conducted with the strain which is the subject of the claim could not be used for the substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship cannot be established between the consumption of *S. cerevisiae* var. *boulardii* CNCM I-3799 and reduction of gastro-intestinal discomfort.

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## BACKGROUND

Regulation (EC) No 1924/2006<sup>4</sup> harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

## STEPS TAKEN BY EFSA

- The application was received on 09/02/2012. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and including a request for the protection of proprietary data.
- The scientific evaluation procedure started on 30/03/2012.
- On 26/04/2012, the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application, and the clock was stopped on 30/04/2012, in compliance with Art. 18(3) of Regulation (EC) No 1924/2006.
- On 21/05/2012, EFSA received the requested information as submitted by the applicant and the clock was restarted.
- During its meeting on 27/06/2012, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort.

## TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort.

## EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of *S. cerevisiae* var. *boulardii* CNCM I-3799, a positive assessment of its safety, nor a decision on whether *S. cerevisiae* var. *boulardii* CNCM I-3799 is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

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<sup>4</sup> Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

## INFORMATION PROVIDED BY THE APPLICANT

### Applicant's name and address:

Lesaffre International / Lesaffre Human Care, 137 rue Gabriel Peri, 59700 Marcq en Baroeul, France.

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006 (unpublished Rousseaux et al. 2009 study).

### Food/constituent as stated by the applicant

According to the applicant, the food constituent for which a health claim is made is *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799, identified as *Saccharomyces boulardii* CNCM I-3799.

### Health relationship as claimed by the applicant

According to the applicant, the relationship between the consumption of *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and maintenance of intestinal comfort has been assessed by evaluating the impact of this strain on the different outcomes of Irritable Bowel Syndrome (IBS). The relationship between the consumption of the yeast and the claimed effect has been evaluated by assessing its impact on the surrogate markers of IBS, particularly abdominal pain, abdominal discomfort, bloating and frequency and consistency of stools. Moreover, the adequate or satisfactory relief of abdominal discomfort has been assessed, both by physicians and subjects. Beyond that, since IBS induces a deterioration of the quality of life of subjects, this outcome has also been evaluated. Thanks to various mechanisms of action, *S. boulardii* CNCM I-3799 significantly enhanced the overall assessment of IBS symptoms and the quality of life of subjects, by reducing the abdominal pain and by improving the stool frequency and consistency.

### Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "*Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 helps maintain intestinal comfort".

### Specific conditions of use as proposed by the applicant

According to the applicant, the target population is male and female, from 18 to 74 years old, with bowel discomfort. The applicant has proposed an intake of  $1 \times 10^{10}$  cfu/day.

## ASSESSMENT

### 1. CHARACTERISATION OF THE FOOD/CONSTITUENT

The food constituent that is the subject of the health claim is *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 (hereafter *S. cerevisiae* var. *boulardii* CNCM I-3799). It was stated in the application that *S. cerevisiae* var. *boulardii* CNCM I-3799 was phenotypically characterised by the biochemical tests of the BIOLOG<sup>®</sup> system. Data on genotypic characterisation of *S. cerevisiae* var. *boulardii* CNCM I-3799, including sequence analysis of the D1/D2 region of the 26S rRNA gene for species identification and PCR inter-delta element analysis for strain typing, were provided in the application.

A culture collection number from the Collection Nationale de Cultures de Microorganismes (CNCM) was provided for *S. cerevisiae* var. *boulardii* CNCM I-3799. The CNCM is a restricted-access non-public collection, which has the status of an International Depositary Authority under the Budapest Treaty.

Data on production, variability of viable yeast counts from batch to batch, stability during storage and other quality control parameters (appearance, water activity, granulometry, biological and chemical safety) of the strain *S. cerevisiae* var. *boulardii* CNCM I-3799 were provided.



The Panel considers that the food constituent, *S. cerevisiae* var. *boulardii* CNCM I-3799, which is the subject of the health claim, is sufficiently characterised.

## 2. RELEVANCE OF THE CLAIMED EFFECT TO HUMAN HEALTH

The claimed effect is “helps maintain intestinal comfort”. The target population proposed by the applicant is “male and female, from 18 to 74 years old, with bowel discomfort”.

The Panel considers that reduction of gastro-intestinal (GI) discomfort is a beneficial physiological effect.

## 3. SCIENTIFIC SUBSTANTIATION OF THE CLAIMED EFFECT

The applicant performed a literature search in Medline, ScienceDirect, Mary Ann Liebert, Springer link, Wiley InterScience, IBIDS, Scirus, and Google scholar with the search terms: “*Saccharomyces cerevisiae* var. *boulardii*” OR “*Saccharomyces boulardii*” OR “*boulardii*” OR “perenterol” OR “hansen CBS 5926” AND “digestive comfort” OR “gut microflora” OR “digestive health” OR “gut” OR “bowel” OR “digest\*” OR “diarrhoea” OR “colitis” OR “diarrhea” OR “fecal microbiota” OR “IBS” OR “Irritable bowel syndrome” OR “Syndrome de l’intestin irritable” OR “SII” OR “Syndrome du colon irritable” OR “spastic colon” OR “functional bowel disorder” OR “abdominal pain” OR “bloating”.

According to the applicant, this literature search resulted in the identification of five human studies which addressed the effects of *S. cerevisiae* var. *boulardii* on functional colopathies (Bennani, 1990), on IBS symptoms (Choi et al., 2011; Maupas et al., 1983), on histology and enzymatic activities (Buts et al., 1986; Jahn et al., 1996) and on lymphocytes (Jahn et al., 1996) of the intestinal mucosa of healthy subjects.

Animal studies submitted addressed the effect of *S. cerevisiae* var. *boulardii* on histology and enzymes of the intestinal mucosa (Buts et al., 1986), on stimulation of secretory IgA production (Buts et al., 1990; Rodriguez et al., 2000) and phagocytic activity (Rodriguez et al., 2000) in the small intestine, on adaptation of intestinal mucosa after enterectomy (Buts et al., 1999), on inflammatory markers in a model of experimental colitis (Foligné et al., 2010) and on anti-inflammatory and analgesic effects on a chemically-induced colitis model (Rousseaux et al., 2009, unpublished).

*In vitro* studies addressing effects of *S. cerevisiae* var. *boulardii* on immune-related parameters in cell cultures (Sougioultzis et al., 2006), and on survival of the strain in simulated GI conditions, adhesion to cell lines and cytokine gene expression in cell cultures (van der Aa Kühle et al., 2005; Denis et al. 2010, unpublished) were also provided.

The Panel notes that none of the studies provided for the substantiation of the claim were conducted with the strain which is the subject of the claim (*S. cerevisiae* var. *boulardii* CNCM I-3799), except for two animal studies and one *in vitro* study (Foligné et al., 2010; Rousseaux et al. 2009, unpublished; Denis et al. 2010, unpublished).

Upon an EFSA request, the applicant indicated that the rest of the studies provided were conducted with the strain produced by Biocodex Laboratories (*S. cerevisiae* var. *boulardii* HANSEN CBS 5926), sold under different brand names. The applicant also stated that the strain, which is the subject of the claim, *S. cerevisiae* var. *boulardii* CNCM I-3799, is equivalent to *S. cerevisiae* var. *boulardii* HANSEN CBS 5926, based on a comparative PCR inter-delta element analysis of both strains provided in the application.

The Panel considered that this evidence was insufficient to establish that the strains *S. cerevisiae* var. *boulardii* CNCM I-3799 and HANSEN CBS 5926 are identical and, upon EFSA request for further information, additional data were not provided by the applicant. The Panel also considered that in the

absence of human data the two animal studies and one *in vitro* study conducted with the strain which is the subject of the claim cannot be used for the substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship cannot be established between the consumption of *S. cerevisiae* var. *boulardii* CNCM I-3799 and reduction of gastro-intestinal discomfort.

## CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799, which is the subject of the claim, is sufficiently characterised.
- The claimed effect is “helps maintain intestinal comfort”. The target population as proposed by the applicant is “male and female, from 18 to 74 years old, with bowel discomfort”. Reducing gastro-intestinal discomfort is a beneficial physiological effect.
- A cause and effect relationship cannot be established between the consumption of *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort.

## DOCUMENTATION PROVIDED TO EFSA

Health claim application on *Saccharomyces cerevisiae* var. *boulardii* CNCM I-3799 and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 327\_FR). March 2012. Submitted by Lesaffre International/Lesaffre Human Care.

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## **GLOSSARY / ABBREVIATIONS**

CNCM Collection Nationale de Cultures de Microorganismes

GI gastro-intestinal

IBS irritable bowel syndrome

PCR polymerase chain reaction